DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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January 29, 2002

Mr. Edwin K. Zechman, Jr.
President & CEO
Children's National Medical Center
111 Michigan Avenue, NW
Washington, D.C. 20010-2970

Mark Batshaw, M.D.
Chief Academic Officer & Director of Children's Research Institute
Children's National Medical Center
111 Michigan Avenue, NW
Washington, D.C. 20010-2970

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1316
Research Project: CCG-0957 - A Limited Institution Phase I Study of B43-PAP Immunotoxin in Combination with Standard 3 Drug Induction for Patients with CD19+ ALL in Relapse
Principal Investigator: Gregory Reaman, M.D.

Dear Mr. Zechman and Dr. Batshaw:

The Office for Human Research Protections (OHRP) has reviewed the Children's National Medical Center (CNMC) report dated January 10, 2002. OHRP has determined that the actions summarized below appropriately address the issues raised in OHRP's letter of November 21, 2001.

(1) OHRP notes that in January, 2000, the CNMC Institutional Review Board (IRB) revised the procedures for continuing review of research. As described in CNMC's revised written

Procedures, for continuing review of research not eligible for expedited review, all IRB members receive and review a protocol summary and a status report on the progress of the research, including (i) the number of subjects accrued; (ii) a description of any adverse events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (iii) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (iv) a copy of the current informed consent document. OHRP notes that the CNMC Continuing Review Committee (CRC) meets prior to a convened IRB meeting to separately review each protocol scheduled for continuing review by the IRB. Each protocol reviewed by the CNMC CRC is presented separately with recommendations by the CRC Chair at the convened IRB meeting. OHRP notes also that in August, 2001, the IRB began voting individually after each protocol has been reviewed and the IRB minutes now document separate deliberations, actions and votes for each protocol undergoing continuing review.

(2) OHRP notes that the CNMC has modified its IRB policies and procedures to include (i) a specific reference to HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5) and outline the requirements for the reporting of any unanticipated problems involving risks to subjects or others; and (ii) a specific reference to the HHS regulation at 45 CFR 46.110(b)(2). In addition, CNMC plans to emphasize the importance of these requirements in education and institutional mentoring programs for investigators on IRB policies and procedures.

(3) OHRP notes CNMC's corrective action plan to develop a general screening protocol for investigational drug studies in children with refractory cancer and an appropriate informed consent document that will clearly delineate all screening procedures which are being performed outside of routine clinical care and solely for the purpose of determination of eligibility. OHRP also notes that CNMC plans to inform potential patients and their physicians from other institutions of specific screening procedures that are required to be performed solely to determine a subjects's eligibility to participate in a clinical research study at CNMC. In the future, these specific screening procedures will be performed exclusively at CNMC.

(4) OHRP notes that in response to the date discrepancies and the omission of pertinent information in the Report of Action letter to the investigator, CNMC plans to modify its administrative procedures and computer system to preclude future problems.

As a result, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Mr. Ron Sloan, CNMC
Dr. John L. Sever, CNMC
Dr. Gregory H. Reaman, CNMC
Commissioner, FDA
Dr. David A. Lepay, FDA
Dr. James F. McCormack, FDA
Ms. Elaine Knowles Cole, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael A. Carome, OHRP
Dr. Jeffrey M. Cohen, OHRP
Mr. George Gasparis, OHRP
Ms. Janice F. Walden, OHRP
Mr. Barry Bowman, OHRP